

GenCore version 4.5  
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OM protein - protein search, using sw model

Run on: July 10, 2002, 08:22:08 ; Search time 30.1 seconds  
(without alignments)  
59.043 Million cell updates/sec

Title: US-09-508-054-19

Perfect score: 87

Sequence: 1 YLRIVQCRSEVSGSGF 16

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 747574 seqs, 11073796 residues

Total number of hits satisfying chosen parameters: 747574

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 150 summaries

Database : A\_Geneseq\_032802.\*

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22: /SIDS1/gcgdata/hold-geneseq/geneseq-emb1/AA2001.DAT.\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	87	100.0	16	AA101663	Peptide analogue 9
2	87	100.0	16	AA173624	Human growth hormo
3	84	96.6	191	AA124050	hGH variant #2 - 1
4	84	96.6	191	AA124052	hGH variant #4 - 1
5	84	96.6	191	AA124053	hGH variant #5 - 1
6	84	96.6	191	AA124055	hGH variant #7 - 1
7	84	96.6	191	AA124057	hGH variant #9 - 1
8	84	96.6	191	AA124059	hGH variant #13 -
9	84	96.6	191	AA124725	hGH variant #14 -
10	84	96.6	191	AA124726	hGH variant #15 -
11	84	96.6	191	AA124729	hGH variant #17 -

84	96.6	191	13	AA124731	hGH variant #19 -
84	96.6	191	13	AA124734	hGH variant #22 -
84	96.6	191	13	AA124737	hGH variant #25 -
84	96.6	191	13	AA124740	hGH variant #28 -
84	96.6	191	13	AA124743	hGH variant #31 -
84	96.6	191	13	AA124751	hGH variant #39 -
84	96.6	191	13	AA124753	hGH variant #41 -
84	96.6	191	13	AA124757	hGH variant #45 -
84	96.6	191	13	AA124762	hGH variant #50 -
84	96.6	191	13	AA124766	hGH variant #54 -
84	96.6	191	13	AA124769	hGH variant #57 -
84	96.6	191	13	AA124776	hGH variant #58 -
84	96.6	191	13	AA124776	hGH variant #64 -
83	95.4	25	21	AA178432	Human growth hormo
83	95.4	56	5	AA140352	Synthetic human gr
83	95.4	65	22	AA123044	Protein #5043 enco
83	95.4	65	22	AA131150	Peptide #5187 enco
83	95.4	176	18	AA126202	20 kDa human growt
83	95.4	176	18	AA126203	20 kDa human growt
83	95.4	176	18	AA123662	Authentic 20-kilod
83	95.4	176	18	AA123661	Authentic 20-kilod
83	95.4	176	19	AA159762	Amino acid sequenc
83	95.4	176	19	AA159761	Amino acid sequenc
83	95.4	177	16	AA176820	hGHV-3(53) growth
83	95.4	190	21	AA184644	Amino acid sequenc
83	95.4	191	7	AA160016	Sequence of human
83	95.4	191	13	AA124754	hGH variant #42 -
83	95.4	191	13	AA124772	hGH variant #60 -
83	95.4	191	18	AA138221	Human growth hormo
83	95.4	191	18	AA138222	Human growth hormo
83	95.4	191	18	AA138220	Human growth hormo
83	95.4	191	19	AA171289	Human growth hormo
83	95.4	191	20	AA115809	Primary amino acid
83	95.4	191	20	AA115810	Tagged human growt
83	95.4	191	20	AA104396	Natural human 22kD
83	95.4	191	22	AA119836	Mutant human 22kDa
83	95.4	192	20	AA190129	Human growth hormo
83	95.4	192	20	AA192266	Human anti-angioge
83	95.4	192	22	AA192264	Human anti-angioge
83	95.4	192	22	AA119835	Recombinant Ala-hu
83	95.4	193	8	AA170260	Met-Asp-human grow
83	95.4	194	20	AA130530	Recombinant human
83	95.4	198	16	AA176819	hGHV-2(88) growth
83	95.4	202	21	AA193637	Amino acid sequenc
83	95.4	203	15	AA149815	20K hGH (42Met)
83	95.4	212	7	AA160234	Sequence of AP sig
83	95.4	214	7	AA160232	Sequence of Escher
83	95.4	214	7	AA160233	Sequence of Escher
83	95.4	214	11	AA105043	Human growth hormo
83	95.4	214	11	AA110425	Synthetic human gr
83	95.4	214	20	AA131766	Human growth hormo
83	95.4	214	20	AA182801	Human growth hormo
83	95.4	214	21	AA178424	Human growth hormo
83	95.4	214	21	AA178460	Human growth hormo
83	95.4	217	4	AA130046	Sequence of human
83	95.4	217	8	AA171058	Sequence of human
83	95.4	217	11	AA105169	Human growth hormo
83	95.4	217	15	AA160516	Human somatotropin
83	95.4	217	16	AA176818	Human growth hormo
83	95.4	217	19	AA168453	Human growth hormo
83	95.4	217	21	AA126769	Secretory cell pro
83	95.4	217	22	AA110340	Human growth hormo
83	95.4	217	22	AA135428	Secretory cell lin
83	95.4	226	15	AA149814	20K hGH (42Ser)
83	95.4	241	20	AA188526	Fusion of killer t
83	95.4	244	12	AA110042	Plasmid pOW885 hum
83	95.4	245	21	AA169791	MWp-MWp20-(His
83	95.4	344	22	AA170473	Npro-hGH fusion pr
83	95.4	407	22	AA149195	Human growth hormo
83	95.4	779	18	AA122719	Human serum albumi
83	95.4	784	18	AA122717	Human serum albumi
83	95.4	789	18	AA122718	Human serum albumi

85	95.4	794	18	AAW22720	Human serum albumin	ID	AAV01663 standard; peptide; 16 AA.
86	94.3	191	13	AAR24732	hGH variant #20 -	XX	
87	93.1	191	13	AAR24058	hGH variant #10 -	AC	AAV01663;
88	92.0	15	17	AAV01512	Human growth hormo	XX	
89	92.0	15	17	AAW03650	Human growth hormo	DT	23-JUN-1999 (first entry)
90	92.0	15	20	AAV01653	Peptide analogue o	XX	Peptide analogue 9604 of carboxy terminal sequence of hGH.
91	92.0	15	20	AAV01655	Peptide analogue o	DE	
92	92.0	15	20	AAV01656	Peptide analogue o	XX	
93	92.0	15	20	AAV01658	Peptide analogue 9	KW	Peptide analogue; human growth hormone; hGH; fat-reducing enzyme;
94	92.0	15	20	AAV01659	Peptide analogue o	KW	hormone-sensitive lipase; fat-producing enzyme; acetyl CoA carboxylase;
95	92.0	15	20	AAV01679	Peptide analogue o	KW	obesity; meat quality.
96	92.0	15	20	AAV01681	Peptide analogue o	XX	Synthetic.
97	92.0	15	20	AAV01660	Peptide analogue 9	OS	Homo sapiens.
98	92.0	16	20	AAV01664	Peptide analogue 9	XX	
99	92.0	17	20	AAV01654	Peptide analogue o	XX	
100	92.0	17	20	AAV01665	Peptide analogue 9	XX	
101	92.0	98	22	AAO06818	Human polypeptide	FH	Key
102	92.0	191	13	AAR24268	Mature human growth	FT	Disulfide-bond 7..14
103	92.0	191	13	AAR24269	Mature human growth	XX	
104	92.0	191	13	AAR24270	Mature human growth	PN	WO9912969-A1.
105	92.0	191	13	AAR24271	Mature human growth	XX	
106	92.0	191	13	AAR24272	Mature human growth	PD	18-MAR-1999.
107	92.0	191	13	AAR24049	hGH variant #1 - 1	XX	
108	92.0	191	13	AAR24051	hGH variant #3 - 1	PF	04-SEP-1998; 98WO-AU00724.
109	92.0	191	13	AAR24054	hGH variant #6 - 1	XX	
110	92.0	191	13	AAR24728	hGH variant #16 -	PR	13-NOV-1997; 97AU-0000398.
111	92.0	191	13	AAV31765	Human placental la	PR	08-SEP-1997; 97AU-0009001.
112	92.0	191	22	AAB49196	Growth hormone act	XX	
113	92.0	191	22	AAB49197	Growth hormone act	PA	(META-) METABOLIC PHARM LTD.
114	92.0	191	22	AAB49198	Growth hormone act	XX	
115	92.0	191	22	AAB49199	Growth hormone act	PI	Jiang W, Ng FM;
116	92.0	192	20	AAW92262	Human anti-angioten	XX	
117	92.0	214	13	AAR22230	Human growth hormo	DR	WPI; 1999-229224/19.
118	90.8	191	13	AAR24056	hGH variant #8 - 1	XX	Peptide analogues of the C-terminus of a growth hormone
119	90.8	191	13	AAR24730	hGH variant #18 -	PT	
120	90.8	191	13	AAR24733	hGH variant #21 -	XX	Claim 16; Page 50; 95pp; English.
121	90.8	191	13	AAR24736	hGH variant #24 -	PS	
122	90.8	191	13	AAR24738	hGH variant #26 -	XX	The present sequence represents a peptide analogue of the carboxy
123	90.8	191	13	AAR24739	hGH variant #27 -	CC	terminal (amino acids 177-191) of human growth hormone (hGH).
124	90.8	191	13	AAR24741	hGH variant #29 -	CC	The peptide analogues can act to stimulate the fat-reducing enzyme
125	90.8	191	13	AAR24742	hGH variant #30 -	CC	hormone-sensitive lipase and inhibit the fat-producing enzyme
126	90.8	191	13	AAR24744	hGH variant #32 -	CC	acetyl CoA carboxylase, both effects being the result of activating
127	90.8	191	13	AAR24747	hGH variant #35 -	CC	production of the second messenger diacylglycerol. The peptide
128	90.8	191	13	AAR24749	hGH variant #37 -	CC	analogues are used to treat obesity, particularly in humans but
129	90.8	191	13	AAR24750	hGH variant #38 -	CC	also to improve meat quality in farm animals.
130	90.8	191	13	AAR24752	hGH variant #40 -	XX	
131	90.8	191	13	AAR24755	hGH variant #43 -	XX	Sequence 16 AA;
132	90.8	191	13	AAR24756	hGH variant #44 -	SQ	
133	90.8	191	13	AAR24760	hGH variant #48 -		
134	90.8	191	13	AAR24764	hGH variant #52 -		Query Match 100.0%; Score 87; DB 20; Length 16;
135	90.8	191	13	AAR24765	hGH variant #53 -		Best Local Similarity 100.0%; Pred. No. 1.1e-06;
136	90.8	191	13	AAR24767	hGH variant #55 -		Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
137	90.8	191	13	AAR24768	hGH variant #56 -		
138	90.8	191	13	AAR24771	hGH variant #59 -		QY 1 YLRIVQCRSVEGSCGF 16
139	90.8	191	13	AAR24773	hGH variant #61 -		
140	90.8	191	13	AAR24774	hGH variant #62 -		Db 1 ylrivqcrsvegscgf 16
141	90.8	191	13	AAR24775	hGH variant #63 -		
142	89.7	176	9	AP82720	Human 20K growth h		RESULT 2
143	89.7	191	13	AAR24748	hGH variant #36 -		AAAB73624
144	89.7	191	13	AAR24758	hGH variant #46 -		ID AAB73624 standard; peptide; 16 AA.
145	89.7	191	13	AAR24761	hGH variant #49 -	XX	
146	89.7	191	20	AAW86013	Human growth hormo	XX	AC AAB73624;
147	89.7	191	21	AAV78425	Human growth hormo	XX	XX AAB73624;
148	89.7	191	22	AAB49200	Growth hormone act	XX	DT 29-AUG-2001 (first entry)
149	89.7	191	22	AAB49201	Growth hormone act	XX	XX Human growth hormone fragment analogue peptide, AOD9604.
150	88.5	15	20	AAV01661	Peptide analogue 9	XX	Human growth hormone analogue peptide; hGH; AOD9604; lipid metabolism;
						KW	modulation; lipolysis stimulation; hormone-sensitive lipase stimulation;
						KW	lipogenesis inhibition; acetyl CoA carboxylase inhibition; obesity;
						KW	functional food; transgenic yeast; fat/lean ratio; food use;
						KW	cyclic.

ALIGNMENTS

```
XX Homo sapiens.
OS Synthetic.
XX
XX Key Location/Qualifiers
XX Disulfide-bond 7..14
XX
XX WO200133977-A1.
XX
XX 17-MAY-2001.
XX
XX 06-NOV-2000; 2000WO-AU01362.
XX
XX 05-NOV-1999; 99AU-0003875.
XX
XX (META-) METABOLIC PHARM LTD.
XX
XX Belyea CI, Ng FM, Vaughan P;
XX
XX WPI; 2001-328876/34.
XX
XX New organisms containing nucleic acid encoding a growth hormone
PT fragment which modulates lipid metabolism are useful to produce dietary
PT aids for obesity and in the meat production industry -
XX
XX Example; Page 32; 54pp; English.
XX
XX The invention relates to novel transgenic organisms useful in the
CC production of functional food and drink products for the treatment
CC or prevention of obesity via the regulation of lipid metabolism. The
CC organisms comprise a polynucleotide encoding a growth hormone fragment
CC capable of stimulating the activity of hormone-sensitive lipase (the key
CC enzyme in lipolysis) and inhibiting acetyl CoA carboxylase (the key
CC enzyme in lipogenesis). The growth hormone fragment preferably contains
CC at least the disulphide-bonded loop of a mammalian growth hormone (but is
CC not the full-length growth hormone) and is optionally linked to an
CC epitope tag or heterologous fusion protein partner. The transgenic
CC organism may be a microorganism used to produce a fermented product
CC (e.g., yeast), or an edible plant or animal or cell thereof. Food or
CC drink made using methods of the invention are used to modify fat/lean
CC ratio, lipid metabolism or food use in a mammal. In particular, the food
CC or drink products may be used to treat or prevent obesity, particularly
CC in humans, and may also be used to improve the fat/lean ration of
CC livestock raised for meat production. In the exemplification of the
CC invention, the human growth hormone (hGH) fragment analogue AOD9604 was
CC expressed in yeast, optionally fused to the FLAG epitope (AAB73625).
CC The present sequence represents AOD9604, which corresponds to Tyr-hGH
CC 177-191.
XX
XX SQ Sequence 16 AA;
XX
XX Query Match 100.0%; Score 87; DB 22; Length 16;
XX Best Local Similarity 100.0%; Pred. No. 1.1e-06;
XX Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
XX
XX QY 1 YLRIVQCRSVESGCGF 16
XX |||||
XX Db 1 YLRIVQCRSVESGCGF 16
XX
XX RESULT 3
XX AAR24050
XX ID AAR24050 standard; Protein; 191 AA.
XX
XX AC AAR24050;
XX
XX DT 08-DEC-1992 (first entry)
XX
XX DE hGH variant #2 - 172Arg 174Ala 176Tyr 178Arg.
XX
XX KW humanised IgG antibody; human growth hormone; hGH; selection;
XX screening.
XX
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XX Homo sapiens.
OS
XX WO209690-A.
XX
XX 11-JUN-1992.
XX
XX 03-DEC-1991; 91WO-US09133.
XX
XX 03-DEC-1990; 90US-0621667.
XX 10-APR-1991; 91US-0683400.
XX 14-JUN-1991; 91US-0715300.
XX 08-AUG-1991; 91US-0743614.
XX
XX (GETH ) GENENTECH INC.
XX
XX Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
XX Matthews DJ, Wells JA;
XX
XX WPI; 1992-217069/26.
XX
XX Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
XX Claim 24; Page 75; 102pp; English.
XX
XX This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
XX SQ Sequence 191 AA;
XX
XX Query Match 96.6%; Score 84; DB 13; Length 191;
XX Best Local Similarity 93.8%; Pred. No. 3.4e-05;
XX Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
XX
XX QY 1 YLRIVQCRSVESGCGF 16
XX |||||
XX Db 176 YLRIVQCRSVESGCGF 191
XX
XX RESULT 4
XX AAR24052
XX ID AAR24052 standard; Protein; 191 AA.
XX
XX AC AAR24052;
XX
XX DT 08-DEC-1992 (first entry)
XX
XX DE hGH variant #4 - 172Arg 174Ser 176Tyr 178Arg.
XX
XX KW humanised IgG antibody; human growth hormone; hGH; selection;
XX screening; ss.
XX
XX OS Homo sapiens.
XX
XX PN WO209690-A.
XX
XX PD 11-JUN-1992.
XX
XX 03-DEC-1991; 91WO-US09133.
XX
XX 03-DEC-1990; 90US-0621667.
XX 10-APR-1991; 91US-0683400.
XX 14-JUN-1991; 91US-0715300.
XX 08-AUG-1991; 91US-0743614.
XX
```

XX PA (GETH ) GENENTECH INC.  
 XX PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 XX PI Matthews DJ, Wells JA;  
 XX XX WPI; 1992-217069/26.  
 XX DR  
 XX PT Selecting and enriching variant proteins - comprises fusing gene  
 XX PT encoding e.g. growth hormone to part of M13 phage coat protein  
 XX PT and mutagenising fusion prior to selection  
 XX PS  
 XX PS Claim 24; Page 75; 102pp; English.  
 XX CC This sequence represents a preferred hGH variant of the invention.  
 XX CC The variants were produced by either random cassette mutagenesis,  
 XX CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 XX CC Some of these hGH variants have stronger affinities for the hGH  
 XX CC receptor and binding protein.  
 XX CC This sequence was not given in the specification but generated from  
 XX CC the known hGH sequence, and the modifications described in the  
 XX CC specification.  
 XX SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 1 YLRIVQCRSVEGSCGF 16  
 Db 176 YLRIMQCRSVEGSCGF 191  
 ||||:|||||||

RESULT 5  
 AAR24053  
 ID AAR24053 standard; Protein; 191 AA.  
 XX AC AAR24053;  
 XX DT 08-DEC-1992 (first entry)  
 XX DE hGH variant #5 - 172Lys 174Ala 176Tyr 178Arg.  
 XX KW humanised IgG antibody; human growth hormone; hGH; selection;  
 XX KW screening; ss.  
 XX OS Homo sapiens.  
 XX PN WO9209690-A.  
 XX PD 11-JUN-1992.  
 XX PF 03-DEC-1991; 91WO-US09133.  
 XX PR 03-DEC-1990; 90US-0621667.  
 XX PR 10-APR-1991; 91US-0683400.  
 XX PR 14-JUN-1991; 91US-0715300.  
 XX PR 08-AUG-1991; 91US-0743614.  
 XX PA (GETH ) GENENTECH INC.  
 XX PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 XX PI Matthews DJ, Wells JA;  
 XX XX WPI; 1992-217069/26.  
 XX DR  
 XX PT Selecting and enriching variant proteins - comprises fusing gene  
 XX PT encoding e.g. growth hormone to part of M13 phage coat protein  
 XX PT and mutagenising fusion prior to selection  
 XX PS Claim 24; Page 75; 102pp; English.

XX CC This sequence represents a preferred hGH variant of the invention.  
 XX CC The variants were produced by either random cassette mutagenesis,  
 XX CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 XX CC Some of these hGH variants have stronger affinities for the hGH  
 XX CC receptor and binding protein.  
 XX CC This sequence was not given in the specification but generated from  
 XX CC the known hGH sequence, and the modifications described in the  
 XX CC specification.  
 XX SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 1 YLRIVQCRSVEGSCGF 16  
 Db 176 YLRIMQCRSVEGSCGF 191  
 ||||:|||||||

RESULT 6  
 AAR24055  
 ID AAR24055 standard; Protein; 191 AA.  
 XX AC AAR24055;  
 XX DT 08-DEC-1992 (first entry)  
 XX DE hGH variant #7 - 172Lys 174Gln 176Tyr 178Arg.  
 XX KW humanised IgG antibody; human growth hormone; hGH; selection;  
 XX KW screening; ss.  
 XX OS Homo sapiens.  
 XX PN WO9209690-A.  
 XX PD 11-JUN-1992.  
 XX PF 03-DEC-1991; 91WO-US09133.  
 XX PR 03-DEC-1990; 90US-0621667.  
 XX PR 10-APR-1991; 91US-0683400.  
 XX PR 14-JUN-1991; 91US-0715300.  
 XX PR 08-AUG-1991; 91US-0743614.  
 XX PA (GETH ) GENENTECH INC.  
 XX PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 XX PI Matthews DJ, Wells JA;  
 XX XX WPI; 1992-217069/26.  
 XX DR  
 XX PT Selecting and enriching variant proteins - comprises fusing gene  
 XX PT encoding e.g. growth hormone to part of M13 phage coat protein  
 XX PT and mutagenising fusion prior to selection  
 XX PS Claim 24; Page 75; 102pp; English.  
 XX CC This sequence represents a preferred hGH variant of the invention.  
 XX CC The variants were produced by either random cassette mutagenesis,  
 XX CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 XX CC Some of these hGH variants have stronger affinities for the hGH  
 XX CC receptor and binding protein.  
 XX CC This sequence was not given in the specification but generated from  
 XX CC the known hGH sequence, and the modifications described in the  
 XX CC specification.  
 XX SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 YLRIMQCRSVEGSCGF 191

## RESULT 7

AAR24057  
 ID AAR24057 standard; Protein; 191 AA.

XX  
 AC AAR24057;

XX  
 DT 08-DEC-1992 (first entry)

XX  
 DE hGH variant #9 - 172Gln 174Arg 176Tyr 178Arg.

XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.

XX  
 OS Homo sapiens.

XX  
 PN WO9209690-A.

XX  
 PD 11-JUN-1992.

XX  
 PF 03-DEC-1991; 91WO-US09133.

XX  
 PR 03-DEC-1990; 90US-0621667.

PR  
 10-APR-1991; 91US-0683400.

PR  
 14-JUN-1991; 91US-0715300.

PR  
 08-AUG-1991; 91US-0743614.

XX  
 PA (GETH ) GENENTECH INC.

XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;

PI  
 Matthews DJ, Wells JA;

XX  
 DR WPI; 1992-217069/26.

XX  
 PT Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection

XX  
 PS Claim 24; Page 75; 102pp; English.

XX  
 CC This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.

CC  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.

XX  
 SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 YLRIMQCRSVEGSCGF 191

## RESULT 8

AAR24725  
 ID AAR24725 standard; Protein; 191 AA.

XX

AC AAR24725;

XX  
 DT 08-DEC-1992 (first entry)

XX  
 DE hGH variant #13 - 10His 14Gly 18Asn 21Asn.

XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.

XX  
 OS Homo sapiens.

XX  
 PN WO9209690-A.

XX  
 PD 11-JUN-1992.

XX  
 PF 03-DEC-1991; 91WO-US09133.

XX  
 PR 03-DEC-1990; 90US-0621667.

PR  
 10-APR-1991; 91US-0683400.

PR  
 14-JUN-1991; 91US-0715300.

PR  
 08-AUG-1991; 91US-0743614.

XX  
 PA (GETH ) GENENTECH INC.

XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;

PI  
 Matthews DJ, Wells JA;

XX  
 DR WPI; 1992-217069/26.

XX  
 PT Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection

XX  
 PS Claim 24; Page 75; 102pp; English.

XX  
 CC This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.

XX  
 SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 YLRIMQCRSVEGSCGF 191

## RESULT 9

AAR24726  
 ID AAR24726 standard; Protein; 191 AA.

XX  
 AC AAR24726;

XX  
 DT 08-DEC-1992 (first entry)

XX  
 DE hGH variant #14 - 10Ala 14Trp 18Asp 21Asn.

XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.

XX  
 OS Homo sapiens.

XX  
 PN WO9209690-A.

XX

PD 11-JUN-1992.  
XX  
PF 03-DEC-1991; 91WO-US09133.  
XX  
PR 03-DEC-1990; 90US-0621667.  
PR 10-APR-1991; 91US-0683400.  
PR 14-JUN-1991; 91US-0715300.  
PR 08-AUG-1991; 91US-0743614.  
XX  
PA (GETH ) GENENTECH INC.  
XX  
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
PI Matthews DJ, Wells JA;  
XX  
DR WPI; 1992-217069/26.  
XX  
XX Selecting and enriching variant proteins - comprises fusing gene  
PT encoding e.g. growth hormone to part of M13 phage coat protein  
PT and mutagenising fusion prior to selection  
XX  
PS Claim 24; Page 75; 102pp; English.  
XX  
XX This sequence represents a preferred hGH variant of the invention.  
CC The variants were produced by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH  
CC receptor and binding protein.  
CC This sequence was not given in the specification but generated from  
CC the known hGH sequence, and the modifications described in the  
CC specification.  
XX  
XX Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
QY 1 YLRIVQCRSVGSCGF 16  
Db 176 YLRIMQCRSVGSCGF 191  
||||:|||||

RESULT 10  
AAR24727  
ID AAR24727 standard; Protein; 191 AA.  
XX  
XX AAR24727;  
AC  
XX  
XX 08-DEC-1992 (first entry)  
DT  
XX  
XX hGH variant #15 - 10Phe 14Ser 18Phe 21Leu.  
DE  
XX  
XX humanised IgG antibody; human growth hormone; hGH; selection;  
KW screening; ss.  
XX  
XX Homo sapiens.  
OS  
XX  
XX WO9209690-A.  
PN  
XX  
XX 11-JUN-1992.  
PD  
XX  
XX 03-DEC-1991; 91WO-US09133.  
PF  
XX  
XX 03-DEC-1990; 90US-0621667.  
PR  
XX  
XX 10-APR-1991; 91US-0683400.  
PR  
XX  
XX 14-JUN-1991; 91US-0715300.  
PR  
XX  
XX 08-AUG-1991; 91US-0743614.  
PR  
XX  
XX (GETH ) GENENTECH INC.  
PA  
XX  
XX Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
PI Matthews DJ, Wells JA;

XX WPI; 1992-217069/26.  
DR  
XX  
XX Selecting and enriching variant proteins - comprises fusing gene  
PT encoding e.g. growth hormone to part of M13 phage coat protein  
PT and mutagenising fusion prior to selection  
XX  
PS Claim 24; Page 75; 102pp; English.  
XX  
XX This sequence represents a preferred hGH variant of the invention.  
CC The variants were produced by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH  
CC receptor and binding protein.  
CC This sequence was not given in the specification but generated from  
CC the known hGH sequence, and the modifications described in the  
CC specification.  
XX  
XX Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
QY 1 YLRIVQCRSVGSCGF 16  
Db 176 YLRIMQCRSVGSCGF 191  
||||:|||||

RESULT 11  
AAR24729  
ID AAR24729 standard; Protein; 191 AA.  
XX  
XX AAR24729;  
AC  
XX  
XX 08-DEC-1992 (first entry)  
DT  
XX  
XX hGH variant #17 - 10Ile 14Asn 18Ile 21Asn.  
DE  
XX  
XX humanised IgG antibody; human growth hormone; hGH; selection;  
KW screening; ss.  
XX  
XX Homo sapiens.  
OS  
XX  
XX WO9209690-A.  
PN  
XX  
XX 11-JUN-1992.  
PD  
XX  
XX 03-DEC-1991; 91WO-US09133.  
PF  
XX  
XX 03-DEC-1990; 90US-0621667.  
PR  
XX  
XX 10-APR-1991; 91US-0683400.  
PR  
XX  
XX 14-JUN-1991; 91US-0715300.  
PR  
XX  
XX 08-AUG-1991; 91US-0743614.  
PR  
XX  
XX (GETH ) GENENTECH INC.  
PA  
XX  
XX Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
PI Matthews DJ, Wells JA;  
XX  
XX WPI; 1992-217069/26.  
DR  
XX  
XX Selecting and enriching variant proteins - comprises fusing gene  
PT encoding e.g. growth hormone to part of M13 phage coat protein  
PT and mutagenising fusion prior to selection  
XX  
PS Claim 24; Page 75; 102pp; English.  
XX  
XX This sequence represents a preferred hGH variant of the invention.  
CC The variants were produced by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH

CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX  
 SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 YLRIVCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 YLRIMQCRSVEGSCGF 191

RESULT 12  
 AAR24731  
 ID AAR24731 standard; Protein; 191 AA.  
 XX  
 AC AAR24731;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #19 - 174Ser 176Tyr 167Glu 171Ser 175Thr 179Ile.  
 XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX  
 OS Homo sapiens.  
 XX  
 PN WO9209690-A.  
 XX  
 PD 11-JUN-1992.  
 XX  
 PF 03-DEC-1991; 91WO-US09133.  
 XX  
 PR 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX  
 PA (GETH ) GENENTECH INC.  
 XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX  
 DR WPI; 1992-217069/26.  
 XX  
 PT Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX  
 PS Claim 24; Page 75; 102pp; English.  
 XX  
 CC This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX  
 SQ Sequence 191 AA;  
 XX  
 Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 YLRIVCRSVEGSCGF 16  
 ||||:|||||||

Db 176 YLRIMQCRSVEGSCGF 191  
 ||||:|||||||  
 RESULT 13  
 AAR24734  
 ID AAR24734 standard; Protein; 191 AA.  
 XX  
 AC AAR24734;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #22 - 174Ser 176 Tyr 167Arg 171Asp 175Ile 179Ile.  
 XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX  
 OS Homo sapiens.  
 XX  
 PN WO9209690-A.  
 XX  
 PD 11-JUN-1992.  
 XX  
 PF 03-DEC-1991; 91WO-US09133.  
 XX  
 PR 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX  
 PA (GETH ) GENENTECH INC.  
 XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX  
 DR WPI; 1992-217069/26.  
 XX  
 PT Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX  
 PS Claim 24; Page 75; 102pp; English.  
 XX  
 CC This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX  
 SQ Sequence 191 AA;  
 XX  
 Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 YLRIVCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 YLRIMQCRSVEGSCGF 191

RESULT 14  
 AAR24737  
 ID AAR24737 standard; Protein; 191 AA.  
 XX  
 AC AAR24737;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #25 - 174S 176Y 10H 14G 18N 21N 167E 171S 175T 179I.

XX humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX Homo sapiens.  
 XX WO9209690-A.  
 PN 11-JUN-1992.  
 PD 03-DEC-1991; 91WO-US09133.  
 XX 03-DEC-1990; 90US-0621667.  
 XX 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX (GETH ) GENENTECH INC.  
 PA Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 XX Matthews DJ, Wells JA;  
 PI WPI; 1992-217069/26.  
 DR Selecting and enriching variant proteins - comprises fusing gene  
 XX encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 PT Claim 24; Page 75; 102pp; English.  
 PS This sequence represents a preferred hGH variant of the invention.  
 XX The variants were produced by digestion of each of the one-helix  
 CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
 CC variant was then isolated and ligated with the small fragment from  
 CC each helix-1 variant to yield a set of new variants.  
 CC The one helix variants were made by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
 CC of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX Sequence 191 AA;  
 SQ

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 YLRIVQCRSVEGSCGF 16  
 DB 176 YLRIMQCRSVEGSCGF 191  
 ||||:|||||||||||

RESULT 15  
 AAR24740  
 ID AAR24740 standard; Protein; 191 AA.  
 XX AAR24740;  
 AC AAR24740;  
 DT 08-DEC-1992 (first entry)  
 XX hGH variant #28 - 174S 176Y 10A 14W 18D 21N 167E 171S 175T 179I.  
 DE humanised IgG antibody; human growth hormone; hGH; selection;  
 XX screening; ss.  
 KW Homo sapiens.  
 OS WO9209690-A.  
 XX

PD 11-JUN-1992.  
 XX 03-DEC-1991; 91WO-US09133.  
 XX 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX (GETH ) GENENTECH INC.  
 PA Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 XX Matthews DJ, Wells JA;  
 PI WPI; 1992-217069/26.  
 DR Selecting and enriching variant proteins - comprises fusing gene  
 XX encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 PT Claim 24; Page 75; 102pp; English.  
 PS This sequence represents a preferred hGH variant of the invention.  
 XX The variants were produced by digestion of each of the one-helix  
 CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
 CC variant was then isolated and ligated with the small fragment from  
 CC each helix-1 variant to yield a set of new variants.  
 CC The one helix variants were made by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
 CC of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX Sequence 191 AA;  
 SQ

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 YLRIVQCRSVEGSCGF 16  
 DB 176 YLRIMQCRSVEGSCGF 191  
 ||||:|||||||||||

RESULT 16  
 AAR24743  
 ID AAR24743 standard; Protein; 191 AA.  
 XX AAR24743;  
 AC AAR24743;  
 DT 08-DEC-1992 (first entry)  
 XX hGH variant #31 - 174S 176Y 10F 14S 18F 21L 167E 171S 175T 179I.  
 DE humanised IgG antibody; human growth hormone; hGH; selection;  
 XX screening; ss.  
 KW Homo sapiens.  
 OS WO9209690-A.  
 PN 11-JUN-1992.  
 PD 03-DEC-1991; 91WO-US09133.  
 XX 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 PR

XX (GETH ) GENENTECH INC.  
 PA Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX WPI; 1992-217069/26.  
 DR  
 XX Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX Claim 24; Page 75; 102pp; English.  
 PS  
 XX This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by digestion of each of the one-helix  
 CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
 CC variant was then isolated and ligated with the small fragment from  
 CC each helix-1 variant to yield a set of new variants.  
 CC The one helix variants were made by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
 CC of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX Sequence 191 AA;  
 SQ

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 ylrinqcrsvegscgf 191

RESULT 17  
 AAR24751  
 ID AAR24751 standard; Protein; 191 AA.  
 XX  
 AC AAR24751;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #39 - 174S 176Y 10A 14S 18T 21N 167R 171D 175T 179I.  
 XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX Homo sapiens.  
 OS  
 XX WO9209690-A.  
 PN  
 PD 11-JUN-1992.  
 XX  
 PF 03-DEC-1991; 91WO-US09133.  
 XX  
 PR 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX  
 PA (GETH ) GENENTECH INC.  
 XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX WPI; 1992-217069/26.  
 DR  
 XX Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX Claim 24; Page 75; 102pp; English.  
 PS  
 XX This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by digestion of each of the one-helix  
 CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
 CC variant was then isolated and ligated with the small fragment from  
 CC each helix-1 variant to yield a set of new variants.  
 CC The one helix variants were made by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
 CC of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX Sequence 191 AA;  
 SQ

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 ylrinqcrsvegscgf 191

RESULT 18  
 AAR24753  
 ID AAR24753 standard; Protein; 191 AA.  
 XX  
 AC AAR24753;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #41 - 174S 176Y 10W 14G 18S 21S 167R 171D 175T 179I.  
 XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX Homo sapiens.  
 OS  
 XX WO9209690-A.  
 PN  
 PD 11-JUN-1992.  
 XX  
 PF 03-DEC-1991; 91WO-US09133.  
 XX  
 PR 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX  
 PA (GETH ) GENENTECH INC.  
 XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX WPI; 1992-217069/26.  
 DR  
 XX Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX Claim 24; Page 75; 102pp; English.  
 PS  
 XX This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by digestion of each of the one-helix

PT Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX Claim 24; Page 75; 102pp; English.  
 PS  
 XX This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by digestion of each of the one-helix  
 CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
 CC variant was then isolated and ligated with the small fragment from  
 CC each helix-1 variant to yield a set of new variants.  
 CC The one helix variants were made by either random cassette mutagenesis,  
 CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
 CC of hGH.  
 CC Some of these hGH variants have stronger affinities for the hGH  
 CC receptor and binding protein.  
 CC This sequence was not given in the specification but generated from  
 CC the known hGH sequence, and the modifications described in the  
 CC specification.  
 XX Sequence 191 AA;  
 SQ

Query Match 96.6%; Score 84; DB 13; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 ||||:|||||||  
 Db 176 ylrinqcrsvegscgf 191

RESULT 18  
 AAR24753  
 ID AAR24753 standard; Protein; 191 AA.  
 XX  
 AC AAR24753;  
 XX  
 DT 08-DEC-1992 (first entry)  
 XX  
 DE hGH variant #41 - 174S 176Y 10W 14G 18S 21S 167R 171D 175T 179I.  
 XX  
 KW humanised IgG antibody; human growth hormone; hGH; selection;  
 KW screening; ss.  
 XX Homo sapiens.  
 OS  
 XX WO9209690-A.  
 PN  
 PD 11-JUN-1992.  
 XX  
 PF 03-DEC-1991; 91WO-US09133.  
 XX  
 PR 03-DEC-1990; 90US-0621667.  
 PR 10-APR-1991; 91US-0683400.  
 PR 14-JUN-1991; 91US-0715300.  
 PR 08-AUG-1991; 91US-0743614.  
 XX  
 PA (GETH ) GENENTECH INC.  
 XX  
 PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
 PI Matthews DJ, Wells JA;  
 XX WPI; 1992-217069/26.  
 DR  
 XX Selecting and enriching variant proteins - comprises fusing gene  
 PT encoding e.g. growth hormone to part of M13 phage coat protein  
 PT and mutagenising fusion prior to selection  
 XX Claim 24; Page 75; 102pp; English.  
 PS  
 XX This sequence represents a preferred hGH variant of the invention.  
 CC The variants were produced by digestion of each of the one-helix

CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
CC variant was then isolated and ligated with the small fragment from  
CC each helix-1 variant to yield a set of new variants.  
CC The one helix variants were made by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
CC of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH  
CC receptor and binding protein.  
CC This sequence was not given in the specification but generated from  
CC the known hGH sequence, and the modifications described in the  
CC specification.  
XX  
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVESGCGF 16  
||||:|||||  
Db 176 ylrimgcrsvsgcgf 191

RESULT 19  
AAR24757  
ID AAR24757 standard; Protein; 191 AA.  
XX  
AC AAR24757;  
XX  
DT 08-DEC-1992 (first entry)  
XX  
DE hGH variant #45 - 174S 176Y 10P 14S 18D 21N 167R 171D 175T 179I.  
XX  
KW humanised IgG antibody; human growth hormone; hGH; selection;  
KW screening; ss.  
XX  
OS Homo sapiens.  
XX  
PN W09209690-A.  
XX  
PD 11-JUN-1992.  
XX  
PF 03-DEC-1991; 91WO-US09133.  
XX  
PR 03-DEC-1990; 90US-0621667.  
XX  
PR 10-APR-1991; 91US-0683400.  
XX  
PR 14-JUN-1991; 91US-0715300.  
XX  
PR 08-AUG-1991; 91US-0743614.  
XX  
PA (GETH ) GENENTECH INC.  
XX  
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
PI Matthews DJ, Wells JA;  
XX  
WPI; 1992-217069/26.  
XX  
PT Selecting and enriching variant proteins - comprises fusing gene  
PT encoding e.g. growth hormone to part of M13 phage coat protein  
PT and mutagenising fusion prior to selection  
XX  
PS Claim 24; Page 75; 102pp; English.  
XX  
CC This sequence represents a preferred hGH variant of the invention.  
CC The variants were produced by digestion of each of the one-helix  
CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
CC variant was then isolated and ligated with the small fragment from  
CC each helix-1 variant to yield a set of new variants.  
CC The one helix variants were made by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
CC of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH  
CC receptor and binding protein.

CC This sequence was not given in the specification but generated from  
CC the known hGH sequence, and the modifications described in the  
CC specification.  
XX  
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;  
Best Local Similarity 93.8%; Pred. No. 3.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVESGCGF 16  
||||:|||||  
Db 176 ylrimgcrsvsgcgf 191

RESULT 20  
AAR24762  
ID AAR24762 standard; Protein; 191 AA.  
XX  
AC AAR24762;  
XX  
DT 08-DEC-1992 (first entry)  
XX  
DE hGH variant #50 - 174S 176Y 10A 14W 18D 21N 167R 171D 175T 179I.  
XX  
KW humanised IgG antibody; human growth hormone; hGH; selection;  
KW screening; ss.  
XX  
OS Homo sapiens.  
XX  
PN W09209690-A.  
XX  
PD 11-JUN-1992.  
XX  
PF 03-DEC-1991; 91WO-US09133.  
XX  
PR 03-DEC-1990; 90US-0621667.  
XX  
PR 10-APR-1991; 91US-0683400.  
XX  
PR 14-JUN-1991; 91US-0715300.  
XX  
PR 08-AUG-1991; 91US-0743614.  
XX  
PA (GETH ) GENENTECH INC.  
XX  
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;  
PI Matthews DJ, Wells JA;  
XX  
WPI; 1992-217069/26.  
XX  
PT Selecting and enriching variant proteins - comprises fusing gene  
PT encoding e.g. growth hormone to part of M13 phage coat protein  
PT and mutagenising fusion prior to selection  
XX  
PS Claim 24; Page 75; 102pp; English.  
XX  
CC This sequence represents a preferred hGH variant of the invention.  
CC The variants were produced by digestion of each of the one-helix  
CC variants with EcoRI and BstXI. The large fragment of each helix-4b  
CC variant was then isolated and ligated with the small fragment from  
CC each helix-1 variant to yield a set of new variants.  
CC The one helix variants were made by either random cassette mutagenesis,  
CC or site directed oligonucleotide mutagenesis within helix-4 and 1  
CC of hGH.  
CC Some of these hGH variants have stronger affinities for the hGH  
CC receptor and binding protein.  
CC This sequence was not given in the specification but generated from  
CC the known hGH sequence, and the modifications described in the  
CC specification.  
XX  
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;



```
DE hGH variant #58 - 174S 176Y 10A 14W 18D 21N 167R 171D 175T 179I.
XX humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX Homo sapiens.
OS
XX WO209690-A..
PN
XX
XX
XX 11-JUN-1992.
XX
XX 03-DEC-1991; 91WO-US09133..
PF
XX 03-DEC-1990; 90US-0621667.
XX 10-APR-1991; 91US-0683400.
PR
XX 14-JUN-1991; 91US-0715300.
PR
XX 08-AUG-1991; 91US-0743614.
XX
XX (GETH ) GENENTECH INC.
PA
XX Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX WPI; 1992-217069/26.
DR
XX Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
PT
XX Claim 24; Page 75; 102pp; English.
PS
XX This sequence represents a preferred hGH variant of the invention.
XX The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
XX Sequence 191 AA;
SQ
Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 1 YLRIVQCRSVEGSCGF 16
DB 176 YLRIMQCRSVEGSCGF 191
RESULT 24
AAR24776
ID AAR24776 standard; Protein; 191 AA.
XX
XX AAR24776;
AC
XX 08-DEC-1992 (first entry)
DT
XX hGH variant #64 - 174S 176Y 10H 14Q 18Y 21S 167R 171D 175T 179I.
DE
XX humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX Homo sapiens.
OS
XX WO209690-A.
PN
```

```
XX 11-JUN-1992.
PD
XX 03-DEC-1991; 91WO-US09133.
PF
XX 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
XX (GETH ) GENENTECH INC.
PA
XX Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX WPI; 1992-217069/26.
DR
XX Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
PT
XX Claim 24; Page 75; 102pp; English.
PS
XX This sequence represents a preferred hGH variant of the invention.
XX The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
XX Sequence 191 AA;
SQ
Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 1 YLRIVQCRSVEGSCGF 16
DB 176 YLRIMQCRSVEGSCGF 191
RESULT 25
AAY78432
ID AAY78432 standard; Peptide; 25 AA.
XX
XX AAY78432;
AC
XX 09-MAY-2000 (first entry)
DT
XX Human growth hormone variant peptide sequence #3.
DE
XX Human growth hormone; hGH; prolactin; placental lactogen;
KW modification; mutagenesis.
KW
XX Homo sapiens.
OS
XX Synthetic.
OS
XX US6013478-A.
XX
XX 11-JAN-2000.
XX
XX 24-JUN-1998; 98US-0104036.
XX
XX 26-OCT-1989; 89US-0428066.
PR
XX 27-APR-1992; 92US-0875204.
PR
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PR 13-OCT-1992; 92US-0960227.  
 PR 02-FEB-1994; 94US-0190723.  
 PR 06-JUN-1995; 95US-0483039.  
 PR 30-JUN-1997; 97US-0903398.  
 PR 28-OCT-1988; 88US-0264611.

XX (GETH ) GENENTECH INC.

XX Wells JA, Cunningham BC;  
 XX WPI; 2000-159873/14.

XX Recombinant production of variant polypeptides, e.g. growth hormone

PT variants with altered receptor specificity, using cells transformed  
 PT with DNA selected by scanning mutagenesis in at least one peptide  
 PT domain

XX Example 8; Fig 7; 83pp; English.

CC The present invention describes the production of a polypeptide variant  
 CC (I) comprising segment substituted and residue substituted growth  
 CC hormone, prolactin or placental lactogens. The method is particularly  
 CC used to produce variants of growth hormone (GH), prolactin or placental  
 CC lactogen, but may also be applied to receptors, interferons, and  
 CC colony-stimulating factors. A particular application is the production  
 CC of human GH variants with altered (decreased or increased) binding  
 CC interaction with the somatogenic receptor, i.e. compounds useful as  
 CC human GH (ant)agonists and which may have higher potency for stimulating  
 CC other human GH receptors, and as standards or tracers in immunoassays  
 CC for human GH. This method of DNA selection identifies the biologically  
 CC active residues in active domains, including those critical for  
 CC interaction with different targets. The present sequence represents a  
 CC human GH variant peptide sequence, which is used in the exemplification  
 CC of the present invention.

XX Sequence 25 AA;

Query Match 95.4%; Score 83; DB 21; Length 25;  
 Best Local Similarity 93.8%; Pred. No. 6.8e-06;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 1 YLRIVQCRSVEGSCGF 16  
 Db 10 flrlvqcrsvsgcf 25

RESULT 26  
 AAP40352  
 ID AAP40352 standard; Protein; 56 AA.

XX AAP40352;

XX 20-JUL-1992 (first entry)

DE Synthetic human growth hormone.

DE Growth hormone.

XX Synthetic.

XX JP59106297-A.

PD 19-JUN-1984.

PF 07-DEC-1982; 82JP-0214230.

PR 07-DEC-1982; 82JP-0214230.

XX (RIKA ) RIKAGAKU KENKYUSHO.

XX WPI; 1984-186334/30.

DR N-PSDB; AAN40263.

XX

PT Prepn. of carboxy-terminated gene of human growth hormone - by  
 PT solid phase condensn. of 3'-ester(s) of desoxyguanosine,  
 PT desoxycytidine, desoxyadenosine and thymidine with dinucleoside.

XX Claim 1; Page 2; 14pp; Japanese.

XX The protein was produced from a synthetic gene prepd. by success-  
 CC ive solid phase condensation of 3'-esters of deoxyguanosine, deoxy-  
 CC cytidine, deoxyadenosine and thymidine with a dinucleoside, to form  
 CC a group of fragments, followed by enzymic 5'-phosphorylation and  
 CC condensation with DNA ligase. The four dNTPs are first converted to  
 CC the corresp. succinates, and each ester is fixed to a 1%-divinyl  
 CC benzene/styrene copolymer to form a solid nucleoside carrier, which  
 CC serves as the starting material for the synthesis of each fragment.  
 CC The carrier is successively condensed with dinucleotides in a  
 CC definite order by the action of a condensation agent such as  
 CC mesitylenesulphonyl-3-nitrotriazolide. Each oligonucleotide prepd.  
 CC in this way is then phosphorylated and coupled with DNA ligase.

XX Sequence 56 AA;

Query Match 95.4%; Score 83; DB 5; Length 56;  
 Best Local Similarity 93.8%; Pred. No. 1.5e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 1 YLRIVQCRSVEGSCGF 16

Db 41 flrlvqcrsvsgcf 56

RESULT 27  
 ABB23044  
 ID ABB23044 standard; Protein; 65 AA.

XX ABB23044;

XX 23-JAN-2002 (first entry)

DE Protein #5043 encoded by probe for measuring heart cell gene expression.

XX Human; gene expression; heart; microarray; vascular system;  
 KW cardiovascular disease; hypertension; cardiac arrhythmia;  
 KW congenital heart disease.

OS Homo sapiens.

XX WO200157274-A2.

XX 09-AUG-2001.

XX 30-JAN-2001; 2001WO-US00666.

PR 04-FEB-2000; 2000US-0180312.

PR 26-MAY-2000; 2000US-0207456.

PR 30-JUN-2000; 2000US-0608408.

PR 03-AUG-2000; 2000US-0632366.

PR 21-SEP-2000; 2000US-0234687.

PR 27-SEP-2000; 2000US-0236359.

PR 04-OCT-2000; 2000GB-0024263.

XX (MOLE-) MOLECULAR DYNAMICS INC.

XX Penn SG, Hanzel DK, Chen W, Rank DR;

XX WPI; 2001-488899/53.

XX Single exon nucleic acid probes for analyzing gene expression in human  
 PT hearts

XX Claim 15; SEQ ID No 24814; 530pp; English.

CC The present invention relates to single exon nucleic acid probes for  
CC measuring human gene expression in a sample derived from human heart (see  
CC ABA21535-ABA41305). The present sequence is a protein encoded by one such  
CC probe. The probes may be used for predicting, measuring and displaying  
CC gene expression in samples derived from the human heart via microarrays.  
CC By measuring gene expression, the probes are useful for predicting,  
CC diagnosing, grading, staging, monitoring and prognosing diseases of the  
CC human heart and vascular system e.g. cardiovascular disease,  
CC hypertension, cardiac arrhythmias and congenital heart disease.  
CC Note: The sequence data for this patent did not form part of the printed  
CC specification, but was obtained in electronic format directly from WIPO  
CC at ftp.wipo.int/pub/published\_pct\_sequences.

XX SQ Sequence 65 AA;

Query Match 95.4%; Score 83; DB 22; Length 65;  
Best Local Similarity 93.8%; Pred. No. 1.7e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
:|||||  
Db 50 flrivqcrsvegscgf 65

RESULT 28  
AAM31150  
ID AAM31150 standard; Protein; 65 AA.  
XX  
AC AAM31150;  
XX  
DT 17-OCT-2001 (first entry)  
XX  
DE Peptide #5187 encoded by probe for measuring placental gene expression.  
XX  
KW Probe; microarray; human; placenta; antenatal diagnosis;  
KW genetic disorder.  
XX  
OS Homo sapiens.  
XX  
PN WO200157272-A2.  
XX  
PD 09-AUG-2001.  
XX  
PF 30-JAN-2001; 2001WO-US00663.  
PR 04-FEB-2000; 2000US-0180312.  
PR 26-MAY-2000; 2000US-0207456.  
PR 30-JUN-2000; 2000US-0608408.  
PR 03-AUG-2000; 2000US-0632366.  
PR 21-SEP-2000; 2000US-0234687.  
PR 27-SEP-2000; 2000US-0236359.  
PR 04-OCT-2000; 2000GB-0024263.  
XX  
PA (MOLE-) MOLECULAR DYNAMICS INC.  
XX  
PI Penn SG, Hanzel DK, Chen W, Rank DR;  
XX  
XX WPI; 2001-488897/53.

PT Human genome-derived single exon nucleic acid probes useful for  
PT analyzing gene expression in human placenta -

XX ClaIm 27; SEQ ID No 31419; 654pp; English.

XX The present invention relates to single exon nucleic acid probes (SENP:  
CC see AAI315-AAI5746). The present sequence is a peptide encoded by one  
CC such probe. The probes are useful for producing a microarray for  
CC predicting, measuring and displaying gene expression in samples derived  
CC from human placenta. The probes are useful for antenatal diagnosis of  
CC human genetic disorders.

XX SQ Sequence 65 AA;

Query Match 95.4%; Score 83; DB 22; Length 65;  
Best Local Similarity 93.8%; Pred. No. 1.7e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
:|||||  
Db 50 flrivqcrsvegscgf 65

RESULT 29  
AAW26202  
ID AAW26202 standard; protein; 176 AA.  
XX  
AC AAW26202;

DT 29-JAN-1998 (first entry)  
XX  
DE 20 kDa human growth hormone (hGH) example 1.

XX Human growth hormone; hGH; pituitary dwarfism; creatinine;  
KW solubility; preparation.  
XX

OS Homo sapiens.

PN EP787497-A2.

XX  
PD 06-AUG-1997.

XX  
PF 30-JAN-1997; 97EP-0300607.

XX  
PR 02-FEB-1996; 96JP-0017342.

XX (MITK ) MITSUI TOATSU CHEM INC.

XX Aoki M, Fukuhara A, Ito T, Kobayashi H, Kusuhashi N;

PI Miyama Y, Sato T, Uchida H;

XX WPI; 1997-387281/36.

XX Human growth hormone of molecular weight 20000 - stabilised and  
PT solubilised by addition of a water-soluble heterocyclic compound,  
PT for use in pituitary dwarfism therapy

XX Disclosure; Page 5; 15pp; English.

XX This peptide is an example of the 20 kDa human growth hormone (hGH).  
CC There are 2 known types of hGH, a 22 kDa hGH and a 20 kDa hGH. Although  
CC the 22 kDa hGH is produced by means of recombinant DNA technology and  
CC used to treat pituitary dwarfism, the 20 kDa hGH has never been produced  
CC on an industrial scale, and has never been used for medical treatment.  
CC The 20 kDa hGH has a very low solubility in water, which may be due to  
CC hydrophobic interaction of protein molecules. A novel pharmaceutical  
CC preparation has been formulated, comprising a 20 kDa hGH (or a derivative  
CC of it) and a water-soluble heterocyclic compound (e.g. creatinine), which  
CC improves the solubility and stability of the hGH. The pharmaceutical  
CC preparations are suitable for injection. The 20 kDa hGH can be  
CC administered with the 22 kDa hGH in the course of pituitary dwarfism  
CC treatment.

XX SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 18; Length 176;  
Best Local Similarity 93.8%; Pred. No. 4.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
:|||||  
Db 161 flrivqcrsvegscgf 176

```
RESULT 30
AAW26203
ID AAW26203 standard; peptide; 176 AA.
XX
AC AAW26203;
XX
DT 29-JAN-1998 (first entry)
XX
DE 20 kDa human growth hormone (hGH) example 2.
XX
KW Human growth hormone; hGH; pituitary dwarfism; creatinine;
KW solubility; preparation.
XX
OS Homo sapiens.
XX
PN EP787497-A2.
XX
PD 06-AUG-1997.
XX
PF 30-JAN-1997; 97EP-0300607.
XX
PR 02-FEB-1996; 96JP-0017342.
XX
PA (MITK ) MITSUI TOATSU CHEM INC.
XX
PI Aoki M, Fukuhara A, Ito T, Kobayashi H, Kusuhashi N;
PI Miyama Y, Sato T, Uchida H;
XX
DR WPI; 1997-387281/36.
XX
PT Human growth hormone of molecular weight 20000 - stabilised and
PT solubilised by addition of a water-soluble heterocyclic compound,
PT for use in pituitary dwarfism therapy
XX
PS Disclosure; Page 6; 15pp; English.
XX
CC This peptide is an example of the 20 kDa human growth hormone (hGH).
CC There are 2 known types of hGH, a 22 kDa hGH and a 20 kDa hGH. Although
CC the 22 kDa hGH is produced by means of recombinant DNA technology and
CC used to treat pituitary dwarfism, the 20 kDa hGH has never been produced
CC on an industrial scale, and has never been used for medical treatment.
CC The 20 kDa hGH has a very low solubility in water, which may be due to
CC hydrophobic interaction of protein molecules. A novel pharmaceutical
CC preparation has been formulated, comprising a 20 kDa hGH (or a derivative
CC of it) and a water-soluble heterocyclic compound (e.g. creatinine), which
CC improves the solubility and stability of the hGH. The pharmaceutical
CC preparations are suitable for injection. The 20 kDa hGH can be
CC administered with the 22 kDa hGH in the course of pituitary dwarfism
CC treatment.
XX
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 18; Length 176;
Best Local Similarity 93.8%; Pred. No. 4.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16
Db 161 flrivqcrsvsgcf 176
:|||||
:|||||

RESULT 31
AAW23662
ID AAW23662 standard; protein; 176 AA.
XX
AC AAW23662;
XX
DT 13-OCT-1997 (first entry)
XX
DE Authentic 20-kilodalton human growth hormone protein.
XX
KW 20kD hGH; human; medicinal; hormone replacement therapy; lipolysis;
KW serum IGF-1 level.
XX
OS Homo sapiens.
XX
PN EP753307-A2.
XX
PD 15-JAN-1997.
XX
PF 01-JUL-1996; 96EP-0304855.
XX
PR 05-DEC-1995; 95JP-0316883.
PR 29-JUN-1995; 95JP-0163572.
PR 29-JUN-1995; 95JP-0163275.
XX
PA (MITK ) MITSUI TOATSU CHEM INC.
```

```
KW serum IGF-1 level.
XX
OS Homo sapiens.
XX
PN EP753307-A2.
XX
PD 15-JAN-1997.
XX
PF 01-JUL-1996; 96EP-0304855.
XX
PR 05-DEC-1995; 95JP-0316883.
PR 29-JUN-1995; 95JP-0163572.
PR 29-JUN-1995; 95JP-0163275.
XX
PA (MITK ) MITSUI TOATSU CHEM INC.
XX
PI Asada N, Honjo M, Horikomi K, Ikeda M, Kamioka T;
XX
DR WPI; 1997-079182/08.
XX
PT Medicaments contg. 20 kD human growth hormone - useful for hormone
PT replacement therapy and to stimulate lipolysis e.g. for improving
PT body compsn.
XX
PS Claim 2; Page 12; 19pp; English.
XX
CC The present sequence represents an authentic 20-kilodalton human
CC growth hormone (20kD hGH) protein. The 20kD hGH is used in medicinal
CC compositions as an effective component and a pharmaceutically
CC acceptable carrier or diluent. The protein can be used for growth
CC hormone replacement therapy in adults, especially hGH-deficient adults,
CC to improve body composition, stimulate lipolysis and/or increase serum
CC IGF-1 levels. The 20 kD hGH has less tendency to induce glucose
CC intolerance than the known 22 kD hGH.
XX
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 18; Length 176;
Best Local Similarity 93.8%; Pred. No. 4.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16
Db 161 flrivqcrsvsgcf 176
:|||||
:|||||

RESULT 32
AAW23661
ID AAW23661 standard; protein; 176 AA.
XX
AC AAW23661;
XX
DT 13-OCT-1997 (first entry)
XX
DE Authentic 20-kilodalton human growth hormone protein.
XX
KW 20kD hGH; human; medicinal; hormone replacement therapy; lipolysis;
KW serum IGF-1 level.
XX
OS Homo sapiens.
XX
PN EP753307-A2.
XX
PD 15-JAN-1997.
XX
PF 01-JUL-1996; 96EP-0304855.
XX
PR 05-DEC-1995; 95JP-0316883.
PR 29-JUN-1995; 95JP-0163572.
PR 29-JUN-1995; 95JP-0163275.
XX
PA (MITK ) MITSUI TOATSU CHEM INC.
```

XX  
PI Asada N, Honjo M, Horikomi K, Ikeda M, Kamioka T;  
XX WPI; 1997-079182/08.  
XX  
XX Medicaments contg. 20 kD human growth hormone - useful for hormone  
PT replacement therapy and to stimulate lipolysis e.g. for improving  
PT body compsn.  
XX  
XX Claim 2; Page 11; 19pp; English.  
XX  
XX The present sequence represents an authentic 20-kilodalton human  
CC growth hormone (20kD hGH) protein. The 20kD hGH is used in medicinal  
CC compositions as an effective component and a pharmaceutically  
CC acceptable carrier or diluent. The protein can be used for growth  
CC hormone replacement therapy in adults, especially hGH-deficient adults,  
CC to improve body composition, stimulate lipolysis and/or increase serum  
CC IGF-I levels. The 20 kD hGH has less tendency to induce glucose  
CC intolerance than the known 22 kD hGH.  
XX  
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 18; Length 176;  
Best Local Similarity 93.8%; Pred. No. 4.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
Db 161 flrivqcrsvvegscgf 176

RESULT 33  
AAW59762  
ID AAW59762 standard; protein; 176 AA.  
XX  
AC AAW59762;  
XX  
XX 12-OCT-1998 (first entry)  
DT  
XX Amino acid sequence of clone 2 of the human growth hormone.  
DE  
XX Human; growth hormone; inhibition; tumour.  
KW  
XX Homo sapiens.  
OS  
XX JP10182699-A.  
PN  
XX 07-JUL-1998.  
PD  
XX  
XX 26-DEC-1996; 96JP-0347433.  
PF  
XX 26-DEC-1996; 96JP-0347433.  
PR  
XX (MITC ) MITSUI PETROCHEM IND CO LTD.  
XX  
XX WPI; 1998-433892/37.  
XX  
XX Human growth hormone agent - useful in preparation of therapeutics  
PT for inhibiting growth of tumours  
PT  
XX Claim 2; Pages 4-5; 6pp; Japanese.  
XX  
XX This is the amino acid sequence of the human growth hormone used in the  
CC method of the invention involving the preparation of therapeutics for  
CC inhibiting tumour growth.  
XX  
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 19; Length 176;  
Best Local Similarity 93.8%; Pred. No. 4.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
Db 161 flrivqcrsvvegscgf 176

RESULT 35  
AAW59762  
ID AAW59762 standard; protein; 177 AA.  
XX  
AC AAW59762;  
XX  
XX 07-DEC-1995 (first entry)  
DT  
XX hGHV-3(53) growth hormone splice variant.  
DE  
XX  
XX Growth hormone; somatotropin; splice variant; hyperpituitism;  
KW hGHV-3(53); gene therapy.  
XX  
XX Homo sapiens.  
OS  
XX Key Location/Qualifiers  
FT Peptide 1..26  
FT /label= sig\_peptide  
XX  
XX W09520398-A.

QY 1 YLRIVQCRSVEGSCGF 16  
Db 161 flrivqcrsvvegscgf 176

RESULT 34  
AAW59761  
ID AAW59761 standard; protein; 176 AA.  
XX  
AC AAW59761;  
XX  
XX 12-OCT-1998 (first entry)  
DT  
XX Amino acid sequence of clone 1 of the human growth hormone.  
DE  
XX Human; growth hormone; inhibition; tumour.  
KW  
XX Homo sapiens.  
OS  
XX JP10182699-A.  
PN  
XX 07-JUL-1998.  
PD  
XX  
XX 26-DEC-1996; 96JP-0347433.  
PF  
XX 26-DEC-1996; 96JP-0347433.  
PR  
XX (MITC ) MITSUI PETROCHEM IND CO LTD.  
XX  
XX WPI; 1998-433892/37.  
XX  
XX Human growth hormone agent - useful in preparation of therapeutics  
PT for inhibiting growth of tumours  
PT  
XX Claim 2; Pages 4-5; 6pp; Japanese.  
XX  
XX This is the amino acid sequence of the human growth hormone used in the  
CC method of the invention involving the preparation of therapeutics for  
CC inhibiting tumour growth.  
XX  
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 19; Length 176;  
Best Local Similarity 93.8%; Pred. No. 4.4e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
Db 161 flrivqcrsvvegscgf 176

RESULT 35  
AAW59762  
ID AAW59762 standard; protein; 177 AA.  
XX  
AC AAW59762;  
XX  
XX 07-DEC-1995 (first entry)  
DT  
XX hGHV-3(53) growth hormone splice variant.  
DE  
XX  
XX Growth hormone; somatotropin; splice variant; hyperpituitism;  
KW hGHV-3(53); gene therapy.  
XX  
XX Homo sapiens.  
OS  
XX Key Location/Qualifiers  
FT Peptide 1..26  
FT /label= sig\_peptide  
XX  
XX W09520398-A.

XX 03-AUG-1995.  
 XX  
 XX 27-JAN-1995; 95WO-US01130.  
 XX  
 XX 27-JAN-1994; 94US-0187756.  
 PR  
 XX (HUMA-) HUMAN GENOME SCI INC.  
 XX  
 XX Adams MD, Coleman TA, Gocayne JD, Rosen CA;  
 PI  
 XX WPI; 1995-275295/36.  
 XX  
 XX N-PSDB; AAQ93150.  
 DR  
 XX  
 XX DNA and protein sequences of new splice variants of human growth  
 PT hormone - useful for diagnosis and treatment of conditions associated  
 PT with abnormal production of growth hormone, eg. Turner's syndrome,  
 PT gigantism and acromegaly.  
 XX  
 XX Claim 21; Page 35-36; 53pp; English.  
 PS  
 XX The hGHV-3(53) cDNA sequence given in AAQ93150 is generated by  
 CC alternative splicing of wild-type hGH pre-mRNA in which the splice donor  
 CC site of exon-2 is fused to exon-3, resulting in removal of 120  
 CC nucleotides. hGHV-3(53) is partic. useful for treatment of  
 CC hyperpituitism.  
 XX  
 XX Sequence 177 AA;  
 SQ

Query Match 95.4%; Score 83; DB 16; Length 177;  
 Best Local Similarity 93.8%; Pred. No. 4.5e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 :|||||  
 Db 162 flrlvqcrsvegscgf 177

RESULT 36  
 AAY84644  
 ID AAY84644 standard; Protein; 190 AA.  
 XX  
 XX AC AAY84644;  
 XX  
 XX 25-JUL-2000 (first entry)  
 DT  
 XX  
 XX Amino acid sequence of des-Phe human growth hormone (hGH).  
 DE  
 XX Human growth hormone; hGH; idiopathic short stature; Turner's syndrome;  
 KW chronic renal failure; Somatotropin Deficiency Syndrome; cachexia;  
 KW adult growth hormone deficiency; acquired immunodeficiency syndrome;  
 KW AIDS.  
 XX  
 XX Homo sapiens.  
 OS  
 XX WO200015664-A1.  
 PN  
 XX 23-MAR-2000.  
 PD  
 XX 10-SEP-1999; 99WO-AU00742.  
 PF  
 XX 10-SEP-1998; 98AU-0005821.  
 PR  
 XX (BRES-) BRESAGEN LTD.  
 PA  
 XX Bastiras S, Robins A;  
 PI  
 XX WPI; 2000-271384/23.  
 DR  
 XX N-PSDB; AAA12724.  
 DR  
 XX des-Phe human growth hormones useful for treating e.g. Somatotropin  
 PT Deficiency Syndrome and cachexia in acquired immunodeficiency syndrome

PT (AIDS) -  
 XX  
 XX Disclosure; Page 15-16; 18pp; English.  
 XX  
 XX The present sequence represents a des-Phe human growth hormone (hGH).  
 CC des-Phe hGH is identical to natural hGH, however the first amino acid  
 CC (phenylalanine) is absent. hGH is a single chain unglycosylated  
 CC protein. des-Phe hGH can be used to treat a range of diseases associated  
 CC with decreased hGH expression in a patient. These include idiopathic  
 CC short stature, Turner's syndrome, chronic renal failure, Somatotropin  
 CC Deficiency Syndrome (adult growth hormone deficiency) and cachexia in  
 CC acquired immunodeficiency syndrome (AIDS).  
 XX  
 XX Sequence 190 AA;  
 SQ

Query Match 95.4%; Score 83; DB 21; Length 190;  
 Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16  
 :|||||  
 Db 175 flrlvqcrsvegscgf 190

RESULT 37  
 AAP60016  
 ID AAP60016 standard; Protein; 191 AA.  
 XX  
 XX AC AAP60016;  
 XX  
 XX 31-JUL-1991 (first entry)  
 DT  
 XX  
 XX Sequence of human growth hormone (BGH).  
 DE  
 XX Somatotropin; somatotrophin.  
 KW  
 XX Homo sapiens.  
 OS  
 XX EP192629-A.  
 PN  
 XX 27-AUG-1986.  
 PD  
 XX 21-FEB-1986; 86EP-0870023.  
 PF  
 XX 22-FEB-1985; 85US-0704677.  
 PR  
 XX 22-FEB-1985; 85US-0704341.  
 PR  
 XX 25-AUG-1986; 86US-0900017.  
 PR  
 XX (MONS ) MONSANTO CO.  
 PA  
 XX Bentle LA, Mitchell JW, Storrs SB, Shimamoto GT;  
 PI  
 XX WPI; 1986-227173/35.  
 DR  
 XX Solubilisation and maturation of heterologous somatotropin - by  
 PT treating refractory bodies with urea or di:methyl-sulphone then  
 PT oxidising  
 PT  
 XX Disclosure; Page 4; 13pp; English.  
 PS  
 XX The patentors claim a method for solubilisation and maturation of  
 CC somatotropin protein from refractile bodies (RB) of a host cell. The  
 CC method is used for maturation of heterologous bovine or porcine  
 CC somatotropins (claimed), partic. expressed by E. coli, giving  
 CC biologically active material.  
 XX  
 XX Sequence 191 AA;  
 SQ

Query Match 95.4%; Score 83; DB 7; Length 191;  
 Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
 Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

```

QY      1 YLRIVQCRSVEGSCGF 16
      :|||||
Db      176 flrvqcrsvegscgf 191

RESULT 38
AAR24754
ID      AAR24754 standard; Protein; 191 AA.
XX
AC      AAR24754;
XX
DT      08-DEC-1992 (first entry)
XX
DE      hGH variant #42 - 174S 176Y 10F 14L 18S 21S 167K 171N 175T 179V.
XX
KW      humanised IgG antibody; human growth hormone; hGH; selection;
KW      screening; ss.
XX
OS      Homo sapiens.
XX
PN      W09209690-A.
XX
XX      11-JUN-1992.
PD
XX
PF      03-DEC-1991; 91WO-US09133.
XX
PR      03-DEC-1990; 90US-0621667.
PR      10-APR-1991; 91US-0683400.
PR      14-JUN-1991; 91US-0715300.
PR      08-AUG-1991; 91US-0743614.
XX
PA      (GETH ) GENENTECH INC.
XX
PI      Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI      Matthews DJ, Wells JA;
XX
XX      WPI; 1992-217069/26.
DR
XX
PT      Selecting and enriching variant proteins - comprises fusing gene
PT      encoding e.g. growth hormone to part of M13 phage coat protein
PT      and mutagenising fusion prior to selection
XX
PS      Claim 24; Page 75; 102pp; English.
XX
CC      This sequence represents a preferred hGH variant of the invention.
CC      The variants were produced by digestion of each of the one-helix
CC      variants with EcoRI and BstXI. The large fragment of each helix-4b
CC      variant was then isolated and ligated with the small fragment from
CC      each helix-1 variant to yield a set of new variants.
CC      The one helix variants were made by either random cassette mutagenesis,
CC      or site directed oligonucleotide mutagenesis within helix-4 and 1
CC      of hGH.
CC      Some of these hGH variants have stronger affinities for the hGH
CC      receptor and binding protein.
CC      This sequence was not given in the specification but generated from
CC      the known hGH sequence, and the modifications described in the
CC      specification.
XX
SQ      Sequence 191 AA;

Query Match      95.4%; Score 83; DB 13; Length 191;
Best Local Similarity 87.5%; Pred. No. 4.8e-05;
Matches 14; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

QY      1 YLRIVQCRSVEGSCGF 16
      :|||||
Db      176 flrvqcrsvegscgf 191

RESULT 39
AAR24772
ID      AAR24772 standard; Protein; 191 AA.
XX
AC      AAR24772;
XX
DT      08-DEC-1992 (first entry)
XX
DE      hGH variant #60 - 174S 176Y 10F 14S 18L 21A 167N 171S 175T 179V.
XX
KW      humanised IgG antibody; human growth hormone; hGH; selection;
KW      screening; ss.
XX
OS      Homo sapiens.
XX
PN      W09209690-A.
XX
XX      11-JUN-1992.
PD
XX
PF      03-DEC-1991; 91WO-US09133.
XX
PR      03-DEC-1990; 90US-0621667.
PR      10-APR-1991; 91US-0683400.
PR      14-JUN-1991; 91US-0715300.
PR      08-AUG-1991; 91US-0743614.
XX
PA      (GETH ) GENENTECH INC.
XX
PI      Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI      Matthews DJ, Wells JA;
XX
XX      WPI; 1992-217069/26.
DR
XX
PT      Selecting and enriching variant proteins - comprises fusing gene
PT      encoding e.g. growth hormone to part of M13 phage coat protein
PT      and mutagenising fusion prior to selection
XX
PS      Claim 24; Page 75; 102pp; English.
XX
CC      This sequence represents a preferred hGH variant of the invention.
CC      The variants were produced by digestion of each of the one-helix
CC      variants with EcoRI and BstXI. The large fragment of each helix-4b
CC      variant was then isolated and ligated with the small fragment from
CC      each helix-1 variant to yield a set of new variants.
CC      The one helix variants were made by either random cassette mutagenesis,
CC      or site directed oligonucleotide mutagenesis within helix-4 and 1
CC      of hGH.
CC      Some of these hGH variants have stronger affinities for the hGH
CC      receptor and binding protein.
CC      This sequence was not given in the specification but generated from
CC      the known hGH sequence, and the modifications described in the
CC      specification.
XX
SQ      Sequence 191 AA;

Query Match      95.4%; Score 83; DB 13; Length 191;
Best Local Similarity 87.5%; Pred. No. 4.8e-05;
Matches 14; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

QY      1 YLRIVQCRSVEGSCGF 16
      :|||||
Db      176 flrvqcrsvegscgf 191

RESULT 39
AAR24772
ID      AAR24772 standard; Protein; 191 AA.
XX
AC      AAR24772;
XX
DT      19-MAR-1998 (first entry)
XX
DE      Human growth hormone mutant Cys53Ala/Arg77Cys.
XX

```

```

ID      AAR24772 standard; Protein; 191 AA.
XX
AC      AAR24772;
XX
DT      08-DEC-1992 (first entry)
XX
DE      hGH variant #60 - 174S 176Y 10F 14S 18L 21A 167N 171S 175T 179V.
XX
KW      humanised IgG antibody; human growth hormone; hGH; selection;
KW      screening; ss.
XX
OS      Homo sapiens.
XX
PN      W09209690-A.
XX
XX      11-JUN-1992.
PD
XX
PF      03-DEC-1991; 91WO-US09133.
XX
PR      03-DEC-1990; 90US-0621667.
PR      10-APR-1991; 91US-0683400.
PR      14-JUN-1991; 91US-0715300.
PR      08-AUG-1991; 91US-0743614.
XX
PA      (GETH ) GENENTECH INC.
XX
PI      Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI      Matthews DJ, Wells JA;
XX
XX      WPI; 1992-217069/26.
DR
XX
PT      Selecting and enriching variant proteins - comprises fusing gene
PT      encoding e.g. growth hormone to part of M13 phage coat protein
PT      and mutagenising fusion prior to selection
XX
PS      Claim 24; Page 75; 102pp; English.
XX
CC      This sequence represents a preferred hGH variant of the invention.
CC      The variants were produced by digestion of each of the one-helix
CC      variants with EcoRI and BstXI. The large fragment of each helix-4b
CC      variant was then isolated and ligated with the small fragment from
CC      each helix-1 variant to yield a set of new variants.
CC      The one helix variants were made by either random cassette mutagenesis,
CC      or site directed oligonucleotide mutagenesis within helix-4 and 1
CC      of hGH.
CC      Some of these hGH variants have stronger affinities for the hGH
CC      receptor and binding protein.
CC      This sequence was not given in the specification but generated from
CC      the known hGH sequence, and the modifications described in the
CC      specification.
XX
SQ      Sequence 191 AA;

Query Match      95.4%; Score 83; DB 13; Length 191;
Best Local Similarity 87.5%; Pred. No. 4.8e-05;
Matches 14; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

QY      1 YLRIVQCRSVEGSCGF 16
      :|||||
Db      176 flrvqcrsvegscgf 191

RESULT 40
AAR38221
ID      AAR38221 standard; Protein; 191 AA.
XX
AC      AAR38221;
XX
DT      19-MAR-1998 (first entry)
XX
DE      Human growth hormone mutant Cys53Ala/Arg77Cys.
XX

```

KW Mutant; human growth hormone; hGH; treatment; gigantism;  
 KW acromegaly; gene therapy.

OS Homo sapiens.

FH Key Location/Qualifiers

FT Misc-difference 53 /note= "wild type Cys replaced by Ala"

FT Misc-difference 77 /note= "wild type Arg replaced by Cys"

FT

XX EP790305-AL.

PN 20-AUG-1997.

XX 12-FEB-1997; 97EP-0300902.

XX 18-JUN-1996; 96JP-0178643.

PR 13-FEB-1996; 96JP-0050940.

XX (JCRP-) JCR PHARM CO LTD.

XX Chihara K;

DR WPI: 1997-404732/38.

DR N-PSDB; AAT95815.

XX Mutant human growth hormone proteins - with increased receptor

PT affinity and reduced hormone activity

XX Claim 2; Page 17; 28pp; English.

XX The present sequence is a mutant human growth hormone (hGH),  
 CC which can be used to treat gigantism or acromegaly, while its DNA  
 CC can be used for gene therapy. The mutant has a higher affinity for  
 CC hGH receptor than wild-type hGH, can inhibit binding of hGH to  
 CC its receptor and has a lower activity than wild-type hGH.

XX Sequence 191 AA;

Query Match 95.4%; Score 83; DB 18; Length 191;

Best Local Similarity 93.8%; Pred. No. 4.8e-05;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16

Db 176 flrivqcrsvegscgf 191

XXXXXXXXXXXXXXXXXXXX

RESULT 41

AAW38222

ID AAW38222 standard; Protein; 191 AA.

XX

AC AAW38222;

XX 19-MAR-1998 (first entry)

XX Human growth hormone mutant Arg77Cys/Cys165Ala.

DE

XX Mutant; human growth hormone; hGH; treatment; gigantism;

KW acromegaly; gene therapy.

XX Homo sapiens.

XX Key Location/Qualifiers

FT Misc-difference 77 /note= "wild type Arg replaced by Cys"

FT Misc-difference 165 /note= "wild type Cys replaced by Ala"

FT

XX EP790305-AL.

XX

PD 20-AUG-1997.

XX 12-FEB-1997; 97EP-0300902.

XX 18-JUN-1996; 96JP-0178643.

PR 13-FEB-1996; 96JP-0050940.

XX (JCRP-) JCR PHARM CO LTD.

XX Chihara K;

XX WPI: 1997-404732/38.

DR N-PSDB; AAT95816.

XX Mutant human growth hormone proteins - with increased receptor

PT affinity and reduced hormone activity

XX Claim 3; Page 18; 28pp; English.

XX The present sequence encodes a mutant human growth hormone (hGH),

CC which can be used to treat gigantism or acromegaly, while its DNA

CC can be used for gene therapy. The mutant has a higher affinity for

CC hGH receptor than wild-type hGH, can inhibit binding of hGH to

CC its receptor and has a lower activity than wild-type hGH.

XX Sequence 191 AA;

SQ

Query Match 95.4%; Score 83; DB 18; Length 191;

Best Local Similarity 93.8%; Pred. No. 4.8e-05;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16

Db 176 flrivqcrsvegscgf 191

XXXXXXXXXXXXXXXXXXXX

RESULT 42

AAW38220

ID AAW38220 standard; Protein; 191 AA.

XX

AC AAW38220;

XX 19-MAR-1998 (first entry)

XX Human growth hormone mutant Arg77Cys.

DE

XX Mutant; human growth hormone; hGH; treatment; gigantism;

KW acromegaly; gene therapy.

XX Homo sapiens.

XX Key Location/Qualifiers

FT Misc-difference 77 /note= "wild type Arg replaced by Cys"

FT

XX EP790305-AL.

XX 20-AUG-1997.

XX 12-FEB-1997; 97EP-0300902.

XX 18-JUN-1996; 96JP-0178643.

PR 13-FEB-1996; 96JP-0050940.

XX (JCRP-) JCR PHARM CO LTD.

XX Chihara K;

XX WPI: 1997-404732/38.

DR N-PSDB; AAT95814.

XX Mutant human growth hormone proteins - with increased receptor

PT affinity and reduced hormone activity

PS Claim 1; Page 16; 28pp; English.

XX The present sequence is a mutant human growth hormone (hGH),  
CC which can be used to treat gigantism or acromegaly, while its DNA  
CC can be used for gene therapy. The mutant has a higher affinity for  
CC hGH receptor than wild-type hGH, can inhibit binding of hGH to  
CC its receptor and has a lower activity than wild-type hGH.

XX Sequence 191 AA;

SQ Query Match 95.4%; Score 83; DB 18; Length 191;

Best Local Similarity 93.8%; Pred. No. 4.8e-05;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16

DB 176 flrvqcrsvsgscgf 191

RESULT 43

AAW71289

ID AAW71289 standard; protein; 191 AA.

XX

AC AAW71289;

XX

DT 25-NOV-1998 (first entry)

XX

DE Human growth hormone amino acid sequence.

XX

KW Human; growth hormone; treatment; pituitary dwarfism; bone fracture;

XX

KW burn.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Disulfide-bond 53..165

FT Disulfide-bond 182..189

XX

PN JP10234386-A.

XX

PD 08-SEP-1998.

XX

PF 25-DEC-1997; 97JP-0356884.

XX

PR 26-DEC-1996; 96JP-0348033.

XX

PA (TAKE ) TAKEDA CHEM IND LTD.

XX

DR WPI; 1998-535038/46.

XX

PT Method for correct folding of growth hormone - useful for treatment

XX

PT of dwarfism, bone fracture and burns

XX

PS Disclosure; Fig 1; 29pp; Japanese.

XX

CC The present sequence represents a human growth hormone. The specification  
CC describes a method for the preparation of an active type growth hormone.  
CC The method comprises obtaining a growth hormone expressed in a  
CC prokaryotic cell host by genetic engineering, and having it refolded in  
CC a redox buffer. The method is useful for obtaining correctly biologically  
CC functioning growth hormone. The active type growth hormone can be  
CC used for the treatment of pituitary dwarfism, bone fracture and burns.

XX Sequence 191 AA;

Query Match

Best Local Similarity 95.4%; Score 83; DB 19; Length 191;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16

DB 176 flrvqcrsvsgscgf 191

RESULT 44

AAV15809

ID AAV15809 standard; protein; 191 AA.

XX

AC AAV15809;

XX

DT 28-JUL-1999 (first entry)

XX

DE Primary amino acid sequence of native human growth hormone.

XX

KW Detection; fluoresce; illegal misuse; growth substance; athlete;

XX

KW domesticated farm animal; cattle; human growth hormone.

XX

OS Homo sapiens.

XX

PN WO9926069-A1.

XX

PD 27-MAY-1999.

XX

PF 16-NOV-1998; 98WO-GB03449.

XX

PR 14-NOV-1997; 97GB-0023955.

XX

PA (GENE-) GENERIC BIOLOGICALS LTD.

XX

PI Atkinson A, Murphy JP;

XX

DR WPI; 1999-338072/28.

XX

PT Use of tagged exogenous polypeptide

XX

PS Disclosure; Fig 1; 38pp; English.

XX

CC The specification describes a method of detecting an exogenously  
CC administered substance from a naturally-occurring endogenous substance,  
CC the exogenous substance being tagged so that it fluoresces differently  
CC from the endogenous one at a suitable wavelength. The tagging may  
CC consist of one or more substitutions in tagged growth hormone  
CC selected from G40Y, F52Y, W86F, Y, L, I or V F103Y or I137Y;

CC The method is used to distinguish between exogenously administered  
CC substances as compared to naturally-occurring endogenous substances.

CC Especially mentioned is the illegal misuse of growth substances by  
CC athletes or in domesticated farm animals e.g. cattle. The present  
CC sequence represents native human growth hormone which may be used  
CC in the method of the invention.

SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 20; Length 191;

Best Local Similarity 93.8%; Pred. No. 4.8e-05;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 YLRIVQCRSVEGSCGF 16

DB 176 flrvqcrsvsgscgf 191

RESULT 45

AAV15810

ID AAV15810 standard; protein; 191 AA.

XX

AC AAV15810;

XX

DT 28-JUL-1999 (first entry)

XX

DE Tagged human growth hormone.

XX

KW Detection; fluoresce; illegal misuse; growth substance; athlete;  
KW domesticated farm animal; cattle; human growth hormone.  
XX Synthetic.  
OS Homo sapiens.  
XX WO9926069-A1.  
XX WO9926069-A1.  
XX PD 27-MAY-1999.  
XX PF 16-NOV-1998; 98WO-GB03449.  
XX PR 14-NOV-1997; 97GB-0023955.  
XX PA (GENE-) GENERIC BIOLOGICALS LTD.  
XX PI Atkinson A, Murphy JP;  
XX DR WPI; 1999-338072/28.  
XX DR N-PSDB; AAX59843.  
XX PT Use of tagged exogenous polypeptide  
XX PS Example 2; Fig 3; 38pp; English.  
XX The specification describes a method of detecting an exogenously  
CC administered substance from a naturally-occurring endogenous substance,  
CC the exogenous substance being tagged so that it fluoresces differently  
CC from the endogenous one at a suitable wavelength. The tagging may  
CC consist of one or more substitutions in tagged growth hormone  
CC selected from G40Y, F52I, W86F, Y, L, I or V F103Y or I137Y;  
CC The method is used to distinguish between exogenously administered  
CC substances as compared to naturally-occurring endogenous substances.  
CC Especially mentioned is the illegal misuse of growth substances by  
CC athletes or in domesticated farm animals e.g. cattle. The present  
CC sequence represents a tagged human growth hormone, which may be used  
CC in the method of the invention.  
XX SQ Sequence 191 AA;  
Query Match 95.4%; Score 83; DB 20; Length 191;  
Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
QY 1 YLRIVQCRSVEGSCGF 16  
Db :|||||  
176 flrlvqcrsvvegscgf 191  
RESULT 46  
AAY04396  
ID AAY04396 standard; protein; 191 AA.  
XX AC AAY04396;  
XX DT 29-JUN-1999 (first entry)  
XX DE Natural human 22kDa growth hormone.  
XX KW Human; 22kDa growth hormone; hGH; mutant; thrombin; resistance;  
XX plasmid; decomposition.  
XX OS Homo sapiens.  
XX PN JP11092499-A.  
XX PD 06-APR-1999.  
XX PF 22-SEP-1997; 97JJP-0275277.  
XX PR 22-SEP-1997; 97JJP-0275277.  
XX PA (SUMU ) SUMITOMO SEIYAKU KK.  
XX DR WPI; 1999-283567/24.  
XX PT A human growth hormone mutant - with equivalent activity to natural  
XX human growth hormone  
XX PS Claim 1; Page 6-7; 10pp; Japanese.  
XX The present invention describes a human growth hormone mutant in which  
CC the 134th Arg and the 135th Thr are replaced respectively by Asp and Pro  
CC in the 1st to the 191st amino acid sequence of natural type human 22 kDa  
CC growth hormone (hGH) and which has a resistance against decomposition by  
CC thrombin. The present sequence represents the mutant hGH. Also  
CC described are: (1) a hGH mutant in which the 134th Arg, the 135th Thr  
CC and the 140th Lys are replaced respectively by Asp, Pro and Ala in the  
CC amino acid sequence of natural type hGH and which has a resistance  
CC against decomposition by thrombin and plasmin; and (2) a drug  
CC preparation containing the above hGH mutant as the active component.  
CC The mutant hGH shows an activity approximately equivalent to that of  
CC natural type hGH and shows a high stability in blood and body fluid.

PA (SUMU ) SUMITOMO SEIYAKU KK.  
XX DR WPI; 1999-283567/24.  
XX PT A human growth hormone mutant - with equivalent activity to natural  
XX human growth hormone  
XX PS Example 1; Page 5-6; 10pp; Japanese.  
XX The present invention describes a human growth hormone mutant in which  
CC the 134th Arg and the 135th Thr are replaced respectively by Asp and Pro  
CC in the 1st to the 191st amino acid sequence of natural type human 22 kDa  
CC growth hormone (hGH) and which has a resistance against decomposition by  
CC thrombin. The present sequence represents the natural hGH. Also  
CC described are: (1) a hGH mutant in which the 134th Arg, the 135th Thr  
CC and the 140th Lys are replaced respectively by Asp, Pro and Ala in the  
CC amino acid sequence of natural type hGH and which has a resistance  
CC against decomposition by thrombin and plasmin; and (2) a drug  
CC preparation containing the above hGH mutant as the active component.  
CC The mutant hGH shows an activity approximately equivalent to that of  
CC natural type hGH and shows a high stability in blood and body fluid.  
XX SQ Sequence 191 AA;  
Query Match 95.4%; Score 83; DB 20; Length 191;  
Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;  
QY 1 YLRIVQCRSVEGSCGF 16  
Db :|||||  
176 flrlvqcrsvvegscgf 191  
RESULT 47  
AAY04397  
ID AAY04397 standard; protein; 191 AA.  
XX AC AAY04397;  
XX DT 29-JUN-1999 (first entry)  
XX DE Mutant human 22kDa growth hormone.  
XX KW Human; 22kDa growth hormone; hGH; mutant; thrombin; resistance;  
XX plasmid; decomposition.  
XX OS Homo sapiens.  
XX PN JP11092499-A.  
XX PD 06-APR-1999.  
XX PF 22-SEP-1997; 97JJP-0275277.  
XX PR 22-SEP-1997; 97JJP-0275277.  
XX PA (SUMU ) SUMITOMO SEIYAKU KK.  
XX DR WPI; 1999-283567/24.  
XX PT A human growth hormone mutant - with equivalent activity to natural  
XX human growth hormone  
XX PS Claim 1; Page 6-7; 10pp; Japanese.  
XX The present invention describes a human growth hormone mutant in which  
CC the 134th Arg and the 135th Thr are replaced respectively by Asp and Pro  
CC in the 1st to the 191st amino acid sequence of natural type human 22 kDa  
CC growth hormone (hGH) and which has a resistance against decomposition by  
CC thrombin. The present sequence represents the mutant hGH. Also  
CC described are: (1) a hGH mutant in which the 134th Arg, the 135th Thr

CC and the 140th Lys are replaced respectively by Asp, Pro and Ala in the  
CC amino acid sequence of natural type hGH and which has a resistance  
CC against decomposition by thrombin and plasmin; and (2) a drug  
CC preparation containing the above hGH mutant as the active component.  
CC The mutant hGH shows an activity approximately equivalent to that of  
CC natural type hGH and shows a high stability in blood and body fluid.  
XX

SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 20; Length 191;  
Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16  
Db 176 flrlvqcrsvsgscgf 191

RESULT 48  
AAB19836  
ID AAB19836 standard; Protein; 191 AA.

XX AAB19836;

DT 05-MAR-2001 (first entry)

DE Human growth hormone.

XX Human growth hormone; somatotropin; hGH; aminopeptidase;  
KW Aeromonas proteolytica; recombinant protein.

XX Homo sapiens.

FH Key Location/Qualifiers  
FT Disulfide-bond 53..165  
FT Disulfide-bond 182..189

XX WO200066761-A2.

XX 09-NOV-2000.

XX 26-APR-2000; 2000MO-US08746.

XX 30-APR-1999; 99US-0132062.

XX (MONS ) MONSANTO CO.

XX Tou JS, Taylor DW;

XX WPI; 2001-015984/02.

XX Removing N-terminal alanyl group from recombinant protein such as human  
PT growth hormone to yield proteins having their native sequences,  
PT involves contacting protein with Aeromonas aminopeptidase -

XX Example 1; Page 24; 48pp; English.

PS The present sequence is that of native human growth hormone (hGH).  
CC This form of the hormone can be obtained from recombinant hGH  
CC having an N-terminal alanine residue (see AAB19835) by in vitro  
CC cleavage using an aminopeptidase from the marine bacterium  
CC Aeromonas proteolytica. This represents an example of the use of  
CC this enzyme to remove N-terminal Ala residues from polypeptides,  
CC especially recombinant proteins, to yield proteins having their  
CC native amino acid sequences. An efficient method for converting  
CC Ala-hGH to hGH involves expression of Ala-hGH in E. coli, recovery  
CC of inclusion bodies, solubilization and refolding in detergent,  
CC detergent removal by ultrafiltration, selective precipitation,  
CC enzyme cleavage and 2 column chromatography steps. The  
CC aminopeptidase can be used in soluble form or immobilized to a  
CC solid support, for reactions carried out in vitro.

XX

SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 22; Length 191;  
Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16  
Db 176 flrlvqcrsvsgscgf 191

RESULT 49  
AAP90129  
ID AAP90129 standard; protein; 192 AA.

XX AAP90129;

XX 06-FEB-1996 (revised)

DT 01-NOV-1989 (first entry)

XX Human growth hormone.

XX Human growth hormone; fusion protein; recombinant  
KW vector.

XX Homo sapiens (Human).

XX JP01144981-A.

XX 07-JUN-1989.

XX 02-DEC-1987; 87JP-0304937.

XX 02-DEC-1987; 87JP-0304937.

XX (WAKU ) WAKUNGA SEIYAKU KK.

XX WPI; 1989-209284/29.

XX N-PSDB; AAN90269.

XX Recombinant vector contg. fusion protein - consisting of human  
PT growth hormone or deriv. ligated to foreign protein, for stability  
PT and high yield.

XX Disclosure; Fig 1; 19pp; Japanese.

XX The invention consists of a vector contg. a fusion protein which is  
CC formed by ligating, downstream of a promoter, hGH or a deriv. (pref.  
CC formed by substn. of Met-14 with Leu) and a foreign protein.  
CC Stability of the vector in the host is greatly increased so the  
CC protein yield is higher.

XX Sequence 192 AA;

Query Match 95.4%; Score 83; DB 10; Length 192;  
Best Local Similarity 93.8%; Pred. No. 4.8e-05;  
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16  
Db 177 flrlvqcrsvsgscgf 192

RESULT 50  
AAW92266  
ID AAW92266 standard; Protein; 192 AA.

XX AAW92266;

XX 08-JUN-1999 (first entry)

XX

DE Human anti-angiogenic peptide hGH-V Met-1Phe191.

XX Human; anti-angiogenic; prolactin; placental lactogen; hPL; angiogenesis;  
KW growth hormone; hGH; hGH-V; capillary endothelial cell proliferation;  
KW placental vascularisation; pregnancy; treatment; angiogenic disease;  
KW tumour; inhibitor; malignant; angiofibroma; arteriovenous malformation;  
KW arthritis; atherosclerotic plaques; corneal graft neovascularisation;  
KW wound healing; proliferative retinopathy; macular degeneration; trachoma;  
KW granuloma; glaucoma; scleritis; uveitis; fracture; Osler-Weber syndrome;  
KW psoriasis; fibroplasia; scleroderma; Kaposi's sarcoma; vascular adhesion;  
KW ulcer; leukaemia; reproductive disorder; contraceptive agent;  
KW gene therapy; pre-eclampsia; intrauterine growth retardation;  
KW placental dysfunction.

XX Homo sapiens.

OS XX

PN WO9851323-A1.

XX 19-NOV-1998.

PD 12-MAY-1998; 98WO-US09691.

XX 13-MAY-1997; 97US-0046394.

XX (REGC ) UNIV CALIFORNIA.

PA Martial JA, Struman I, Taylor R, Weiner RI;

PI WPI; 1999-045192/04.

XX N-PSDB; AAX01710.

XX New anti-angiogenic peptides - comprise N-terminal fragments of

PT human placental lactogen, human growth hormone, growth hormone

PT variant or human prolactin

XX Example 3; Page 51-52; 87pp; English.

PS This invention describes novel human anti-angiogenic peptides derived

XX from 10 to 150 consecutive amino acids selected from the N-terminal end

CC of human placental lactogen (hPL), human growth hormone (hGH), growth

CC hormone variant (hGH-V), or human prolactin. Such peptides (i) inhibit

CC capillary endothelial cell proliferation and organisation (ii) inhibit

CC angiogenesis in chick chorioallantoic membrane and (iii) binds to at

CC least one specific receptor which does not bind an intact full length

CC hGH, hPL, prolactin or hGH-V. The invention also describes a method for

CC diagnosing a probable abnormality of placental vascularisation during

CC pregnancy. The peptides can be used for treating an angiogenic disease in

CC a subject, for inhibiting tumour formation or growth in a patient or for

CC modulating vascularisation of a patient's placenta. In particular, the

CC peptides can be used for preventing or treating e.g. malignant tumours,

CC angiofibroma, arteriovenous malformation, arthritic such as rheumatoid

CC arthritis, atherosclerotic plaques, corneal graft neovascularisation,

CC delayed wound healing, proliferative retinopathy such as diabetic

CC retinopathy, macular degeneration, granulations such as those occurring

CC in haemophilic joints, inappropriate vascularisation in wound healing

CC such as hypertrophic scars or keloid scars, neovascular glaucoma, ocular

CC tumour, uveitis, non-union fractures, Osler-Weber syndrome, psoriasis,

CC pyogenic glaucoma, retrolental fibroplasia, scleroderma, solid tumours,

CC Kaposi's sarcoma, trachoma, vascular adhesions, chronic varicose ulcers,

CC leukaemia, and reproductive disorders such as follicular and luteal cysts

CC and choriocarcinoma. They can also be used as contraceptive agents. DNA

CC encoding the peptides can be used in gene therapy. The measurement of

CC abnormal levels of N-terminal fragments of hGH, hGH-V, prolactin or hPL

CC can be used in assays for impairment of vascular development associated

CC with pre-eclampsia, intrauterine growth retardation, and placental

CC dysfunction.

XX Sequence 192 AA;

SQ

Query Match 95.4%; Score 83; DB 20; Length 192;

Best Local Similarity 93.8%; Pred. No. 4.8e-05;

Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 1 YLRIVQCRSVGSGCF 16

:|||||||

Db 177 flrivqcrsvgscgf 192

Search completed: July 10, 2002, 08:25:19

Job time: 191 sec

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